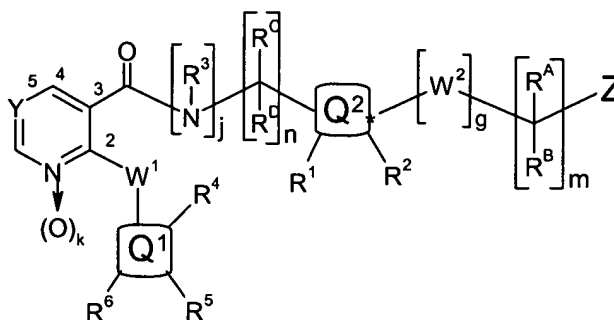


-Amendments to the Claims-

1. (Currently amended) A compound of Formula (1.0.0):



(1.0.0)

— wherein —

- g is 0 or 1;
- j is 0 or 1; provided that when j is 0, n must be 2;
- k is 0 or 1
- m is 0, 1, or 2;
- n is 1 or 2;
- W¹ is -O-; or -S(=O)_t, where t is 0, 1, or 2; or -N(R³)- where R³ has the same meaning as defined below;
- W² is -O-; -S(=O)_t, where t is 0, 1, or 2; -N(R³)- where R³ has the same meaning as defined below, or -CR²⁹R³⁰-;

—where—

- R²⁹ and R³⁰ are each a member independently selected from the group consisting of H; F; CF₃; (C₁-C₃) alkyl; (C₃-C₆) cycloalkyl; phenyl benzyl; and pyridyl; wherein said alkyl, cycloalkyl, phenyl, or benzyl, and pyridyl moieties are each independently substituted with 0 to 3 substituents R¹⁰, where R¹⁰ has the same meaning as defined below;

- Y is =C(R^{1a})-, where R^{1a} has the same meaning as defined below; or -[N(=O)]_k- where k is 0 or 1;

—where—

--R¹_a is a member selected from the group consisting of -H; -F; -Cl; -CN; -NO₂; -(C₁-C₄) alkyl; -(C₂-C₄) alkynyl; fluorinated-(C₁-C₃) alkyl; fluorinated-(C₁-C₃) alkoxy; -OR¹⁶; and -C(=O)NR²²_aR²²_b;

— where —

--R²²_a and R²²_b are each independently -H; -CH₃; -CH₂CH₃; -CH₂CH₂CH₃; -CH₂(CH₃)₂; -CH₂CH₂CH₂CH₃; -CH(CH₃)CH₂CH₃; -CH₂CH(CH₃)₂; -C(CH₃)₃; cyclopropyl; cyclobutyl; or cyclopentyl;

-R^A and R^B are each a member independently selected from the group consisting of -H; -F; -CF₃; -(C₁-C₄) alkyl; -(C₃-C₇) cycloalkyl; phenyl; and benzyl; wherein said cycloalkyl, phenyl, and benzyl moieties are each independently substituted with 0 to 3 substituents R¹⁰;

— where —

--R¹⁰ is a member selected from the group consisting of phenyl; ~~pyridyl~~; -F; -Cl; -CF₃; oxo (=O); -OR¹⁶; -NO₂; -CN; -C(=O)OR¹⁶; -O-C(=O)R¹⁶; -C(=O)NR¹⁶R¹⁷; -O-C(=O)NR¹⁶R¹⁷; -NR¹⁶R¹⁷; -NR¹⁶C(=O)R¹⁷; -NR¹⁶C(=O)OR¹⁷; -NR¹⁶S(=O)₂R¹⁷; and -S(=O)₂NR¹⁶R¹⁷; where said phenyl or ~~pyridyl~~ is substituted by 0 to 3 R¹¹;

— where —

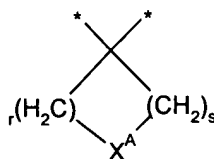
--R¹¹ is -F; -Cl; -CF₃; -CN; -NO₂; -OH; -(C₁-C₃) alkoxy; -(C₁-C₃) alkyl; or -NR¹⁶R¹⁷;

— and —

---R¹⁶ and R¹⁷ are each a member independently selected from the group consisting of -H; -(C₁-C₄) alkyl; -(C₂-C₄) alkenyl; -(C₃-C₆) cycloalkyl; phenyl; and benzyl; ~~and pyridyl~~; wherein said alkyl, alkenyl, cycloalkyl, phenyl, or benzyl, ~~or pyridyl~~ is substituted by 0 to 3 substituents selected from the group consisting of -F, -Cl, -CF₃, -CN, and -(C₁-C₃) alkyl;

— or —

-R^A and R^B are taken together, but only in the case where m is 1, to form a spiro moiety of Formula (1.2.0):



(1.2.0)

— where —

--r and s are independently 0 to 4 provided that the sum of r + s is at least 1 but not greater than 5;

— and —

--X^A is selected from --CH₂--, --CH(R¹¹)--, or C(R¹¹)₂--, where each R¹¹ is selected independently of the other and each has the same meaning as defined above; ~~NR¹⁶--, where R¹⁶ has the same meaning as defined below; --O--; and --S(=O)_t--, where t is 0, 1, or 2;~~

— and —

said spiro moiety of partial Formula (1.2.0) is substituted as to any one or more carbon atoms thereof, other than that defining X^A, by 0 to 3 substituents R¹⁴, where R¹⁴ has the same meaning as defined below; ~~as to a nitrogen atom thereof by 0 or 1 substituent R¹⁵, where R¹⁵ has the same meaning as defined below; and as to a sulfur atom thereof by 0 or 2 oxygen atoms;~~

-R^C and R^D have the same meaning as defined above for R^A and R^B except that one of R^C or R^D ~~them~~ must be -H, and R^C and R^D ~~they~~ are selected independently of each other and of R^A and R^B;

-R¹ and R² may individually or together appear on any ring or rings comprising a meaning of the moiety Q² as defined below; and R¹ and R² are each a member independently selected from the group consisting of -H; -F; -Cl; -CN; -NO₂; -(C₁-C₄) alkyl; -(C₂-C₄) alkynyl; fluorinated-(C₁-C₃) alkyl; -OR¹⁶; and -C(=O)NR²²_aR²²_b; ~~where R¹⁶, R²²_a, and R²²_b have the same meanings as defined above;~~

-R³ is -H; -(C₁-C₃) alkyl; phenyl; benzyl; ~~or -OR¹⁶, where R¹⁶ has the same meaning as defined above;~~

~~-R⁴, R⁵ and R⁶ may individually or together appear on any ring or rings comprising a meaning of the moiety Q¹ as defined below; and~~

~~R⁴, R⁵ and R⁶ are each a member independently~~ is selected from the group consisting of

— the following: —

-(a) -H; -F; -Cl; -(C₂-C₄) alkynyl; -R¹⁶; -OR¹⁶; -S(=O)_pR¹⁶; -C(=O)R¹⁶; -C(=O)OR¹⁶; -OC(=O)R¹⁶; -CN; -NO₂; -C(=O)NR¹⁶R¹⁷; -OC(=O)NR¹⁶R¹⁷; -NR²²_aC(=O)NR¹⁶R¹⁷; -NR²²_aC(=NR¹²)NR¹⁶R¹⁷; -NR²²_aC(=NCN)NR¹⁶R¹⁷; -NR²²_aC(=N-NO₂)NR¹⁶R¹⁷; -C(=NR²²_a)NR¹⁶R¹⁷; -CH₂C(=NR²²_a)NR¹⁶R¹⁷; -OC(=NR²²_a)NR¹⁶R¹⁷; -OC(=N-NO₂)NR¹⁶R¹⁷; -NR¹⁶R¹⁷; -CH₂NR¹⁶R¹⁷; -NR²²_aC(=O)R¹⁶; -NR²²_aC(=O)OR¹⁶; =NOR¹⁶; -NR²²_aS(=O)_pR¹⁷; -S(=O)_pNR¹⁶R¹⁷; and -CH₂C(=NR²²_a)NR¹⁶R¹⁷;

— where —

--p is 0, 1, or 2; and R²²_a, R¹⁶, and R¹⁷ have the same meanings as defined above;

-(b) -(C₁-C₄) alkyl; and -(C₁-C₄) alkoxy in the case where ~~one or more of R⁴, R⁵, or R⁶~~ has the meaning of -OR¹⁶ under (a) above and R¹⁶ is defined as -(C₁-C₄) alkyl; wherein said alkyl and alkoxy are each independently substituted with 0 to 3 substituents -F or -Cl; or 0 or 1 substituent (C₁-C₂) alkoxycarbonyl-; (C₁-C₂) alkylcarbonyl-; or (C₁-C₂) alkylcarbonyloxy-;

— and —

~~-(c) an aryl or heterocyclyl moiety selected from the group consisting of phenyl [[:]] or benzyl; furanyl; tetrahydrofuranyl; oxetanyl; thienyl; tetrahydrothienyl; pyrrolyl; pyrrolidinyl; oxazolyl; oxazolidinyl; isoxazolyl; isoxazolidinyl; thiazolyl; thiazolidinyl; isothiazolyl; isothiazolidinyl; pyrazolyl; pyrazolidinyl; oxadiazolyl; thiadiazolyl; imidazolyl; imidazolidinyl; pyridinyl; pyrazinyl; pyrimidinyl; pyridazinyl; piperidinyl; piperazinyl; triazolyl; triazinyl; tetrazolyl; pyranyl; azetidyl; morpholinyl; parathiazinyl; indolyl; indolinyl; benzo[b]furanyl; 2,3-dihydrobenzofuranyl; 2-H chromenyl; chromanyl; benzothienyl; 1-H indazolyl; benzimidazolyl; benzoxazolyl; benzisoxazolyl; benzthiazolyl; quinolinyl; isoquinolinyl; phthalazinyl; quinazolinyl; quinoxalyl; and purinyl; wherein said phenyl or benzyl aryl and heterocyclyl moieties are each independently substituted with 0 to 2 substituents R¹⁴;~~

— where —

~~--R¹⁴ is a member selected from the group consisting of -(C₁-C₄) alkyl; -(C₃-C₇) cycloalkyl; phenyl; and benzyl; pyridyl; and quinolinyl; where said alkyl, cycloalkyl, phenyl, or benzyl, pyridyl, or quinolinyl is substituted by 0, 1, or 2 substituents -F, -Cl, -CH₃, -OR¹⁶, -NO₂, -CN, or -NR¹⁶R¹⁷; and said R¹⁴ group further consists of -F; -Cl; -CF₃; oxo (=O); -OR¹⁶; -NO₂; -CN; -C(=O)OR¹⁶; -O-C(=O)R¹⁶; -C(=O)NR¹⁶R¹⁷; -O-C(=O)NR¹⁶R¹⁷; -NR¹⁶R¹⁷; -NR¹⁶C(=O)R¹⁷; -NR¹⁶C(=O)OR¹⁷; -NR¹⁶S(=O)₂R¹⁷; or -S(=O)₂NR¹⁶R¹⁷; where R¹⁶ and R¹⁷ have the same meanings as defined above;~~

— and further where —

~~--R¹⁶ is a member independently selected from the group consisting of -H; -NR¹⁶R¹⁷; -C(=O)R¹⁶; -OR¹⁶; -(C₁-C₄) alkyl; -C(=O)OR¹⁶; -(C₁-C₂) alkyl; -C(=O)NR¹⁶R¹⁷; -(C₁-C₄) alkyl; -(C₂-C₄) alkenyl; (CH₂)_u-(C₃-C₇) cycloalkyl where u is 0, 1 or 2; phenyl; and benzyl; pyridyl; and quinolinyl; wherein said alkyl, alkenyl, alkoxy, cycloalkyl, phenyl, or benzyl, pyridyl or quinolinyl is substituted with 0 to 3 substituents R¹²; where R¹⁶ and R¹⁷ have the same meanings as defined above; and~~

— where —

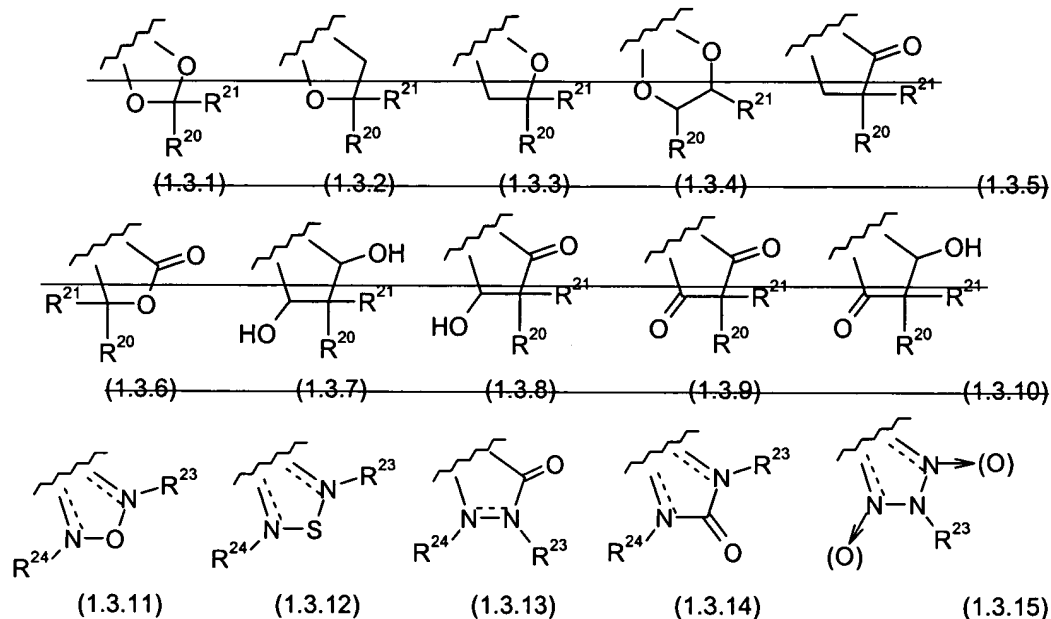
~~----R¹² is a member independently selected from the group consisting of -F; -Cl; -CO₂R¹⁸; -OR¹⁶; -CN; -C(=O)NR¹⁸R¹⁹; -NR¹⁸R¹⁹; -NR¹⁸C(=O)R¹⁹; -NR¹⁸C(=O)OR¹⁹; -NR¹⁸S(=O)_pR¹⁹; -S(=O)_pNR¹⁸R¹⁹, where p is 1 or 2; -(C₁-C₄) alkyl; and -(C₁-C₄) alkoxy in the case where R¹² has the meaning of -OR¹⁶ above and R¹⁶ is defined as -(C₁-C₄) alkyl; wherein said alkyl and alkoxy are each independently substituted with 0 to 3 substituents independently selected from -F; -Cl; -(C₁-C₂) alkoxycarbonyl; -(C₁-C₂) alkylcarbonyl; and -(C₁-C₂) alkylcarbonyloxy; where R¹⁶ has the same meaning as defined above; and~~

— where —

~~-----R¹⁸ and R¹⁹ are independently selected from the group consisting of -H; -(C₁-C₄) alkyl; and phenyl; where said alkyl or phenyl is substituted by 0-3 of -F; or -Cl;~~

— or in the case where Q' is phenyl —

-(d) R^5 and R^6 are taken together to form a moiety which is a member selected from the group consisting of partial Formulas (1.3.11) through (1.3.15) (1.3.1) through (1.3.15):



— wherein —

R^{20} and R^{21} are each a member independently selected from the group consisting of H ; F ; Cl ; CH_3 ; CH_2F ; CHF_2 ; CF_3 ; OCH_3 ; and OCF_3 ;

R^{23} and R^{24} are each independently H ; CH_3 ; OCH_3 ; CH_2CH_3 ; OCH_2CH_3 ; $CH_2CH_2CH_3$; $CH_2(CH_3)_2$; $CH_2CH_2CH_2CH_3$; $CH(CH_3)CH_2CH_3$; $CH_2CH(CH_3)_2$; $C(CH_3)_3$; or absent, in which case the dashed line — — — represents a double bond;

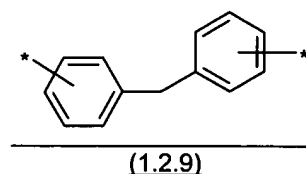
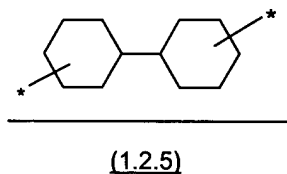
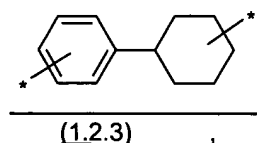
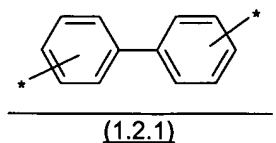
Q' is phenyl a moiety comprising a saturated or unsaturated carbon ring system that is a 3 to 7 membered monocyclic, or that is a 7 to 12 membered, fused polycyclic; provided that Q' is not a discontinuous or restricted biaryl moiety as defined under Q^2 below; and wherein optionally one carbon atom of said carbon ring system may be replaced by a heteroatom selected from N, O, and S; where optionally a second carbon atom thereof, and further optionally a third carbon atom thereof may be replaced by N;

— wherein —

said phenyl moiety defining Q' is substituted on any ring or rings thereof by R^4 , R^5 and R^6 , which have the same meaning as defined above;

Q^2 is a discontinuous or restricted biaryl moiety consisting of a saturated or unsaturated carbon ring system that is a 3 to 7 membered monocyclic, or that is a 7 to 12 membered, fused polycyclic; wherein optionally one carbon atom of said carbon ring system

may be replaced by a heteroatom selected from N, O, and S; where optionally a second carbon atom thereof, and further optionally a third carbon atom thereof may be replaced by N;

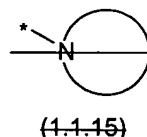
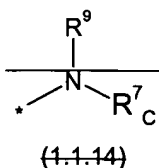
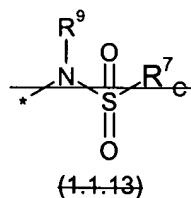
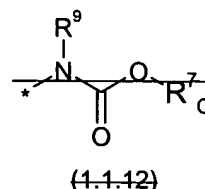
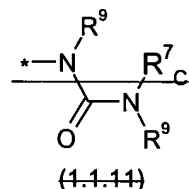
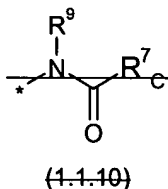
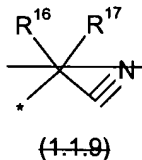
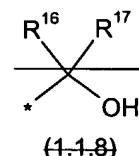
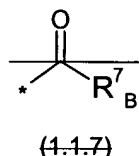
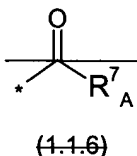
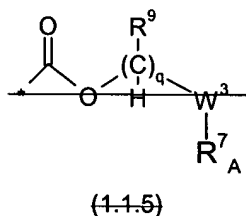
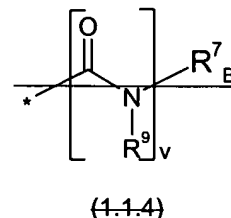
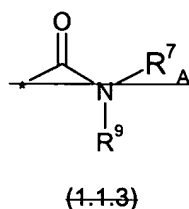
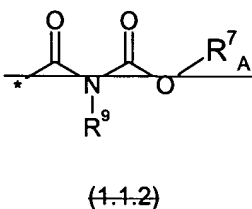
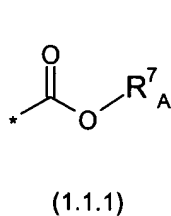


or

-Z is a member independently selected from the group consisting of

— the following —

-(a) — the group consisting of partial Formulas (1.1.1) through (1.1.15):



— wherein —

where R^{16} and R^{17} have the same meanings as defined above; and R^9 has the same meaning as defined below;

--"*" indicates the point of attachment of each partial Formula (1.1.1) through (1.1.15) to the remaining portion of Formula (1.0.0);

~~—q— is 1, 2, or 3, provided that where q is 2 or 3, R^9 has the meaning of H in at least one instance, or two instances, respectively;~~

~~—v— 0 or 1;~~

~~— W^3 — is O ; $N(R^9)$, where R^9 has the same meaning as defined below; or $OC(=O)$ —;~~

~~— R_A^7 is a member independently selected from the group consisting of~~

~~— the following: —~~

~~—(1) —H;~~

~~—(2) —(C_1 - C_6) alkyl; —(C_2 - C_6) alkenyl; or —(C_2 - C_6) alkynyl; where said alkyl, alkenyl or alkynyl is substituted by 0 to 3 substituents R^{10} , where R^{10} has the same meaning as defined above;~~

~~—(3) —(CH_2)_u-(C_3 - C_7) cycloalkyl; where u is 0, 1 or 2; and further where said (C_3 - C_7) cycloalkyl is substituted by 0 to 3 substituents R^{10} where R^{10} has the same meaning as defined above;~~

~~— and —~~

~~—(4) phenyl or benzyl, where said phenyl or benzyl is independently substituted by 0 to 3 substituents R^{10} where R^{10} has the same meaning as defined above;~~

~~— R_B^7 — is a member independently selected from the group consisting of~~

~~— the following: —~~

~~—(1) —tetrazol-5-yl; 1,2,4-triazol-3-yl; 1,2,4-triazol-3-on-5-yl; 1,2,3-triazol-5-yl; imidazol-2-yl; imidazol-4-yl; imidazolidin-2-on-4-yl; 1,3,4-oxadiazolyl; 1,3,4-oxadiazol-2-on-5-yl; 1,2,4-oxadiazol-3-yl; 1,2,4-oxadiazol-5-on-3-yl; 1,2,4-oxadiazol-5-yl; 1,2,4-oxadiazol-3-on-5-yl; 1,2,5-thiadiazolyl; 1,3,4-thiadiazolyl; morpholinyl; parathiazinyl; oxazolyl; isoxazolyl; thiazolyl; isothiazolyl; pyrrolyl; pyrazolyl; succinimidyl; glutarimidyl; pyrrolidonyl; 2-piperidonyl; 2-pyridonyl; 4-pyridonyl; pyridazin-3-onyl; pyridyl; pyrimidinyl; pyrazinyl; pyridazinyl;~~

~~— and —~~

~~—(2) —indolyl; indolinyl; isoindolinyl; benzo[b]furanyl; 2,3-dihydrobenzofuranyl; 1,3-dihydroisobenzofuranyl; 2H-1-benzopyranyl; 2-H-chromenyl; chromanyl; benzothienyl; 1H-indazolyl; benzimidazolyl; benzoxazolyl; benzisoxazolyl; benzothiazolyl; benzotriazolyl;~~

~~benzotriazinyl; phthalazinyl; 1,8-naphthyridinyl; quinoliny; isoquinoliny; quinazolinyl; quinoxaliny; pyrazolo[3,4-d]pyrimidinyl; pyrimido[4,5-d]pyrimidinyl; imidazo[1,2-a]pyridinyl; pyridopyridinyl; pteridinyl; and 1H-purinyl;~~

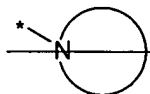
~~—where—~~

~~any moiety recited in (1) or (2) above is optionally substituted with respect to (i) any one or more carbon atoms thereof optionally by a substituent R^{14} where R^{14} has the same meaning as defined above; (ii) any one or more nitrogen atoms thereof that is not a point of attachment of said moiety, optionally by a substituent R^{15} where R^{15} has the same meaning as defined above, and all tautomer forms thereof; and (iii) any sulfur atom thereof that is not a point of attachment of said moiety, by 0, 1, or 2 oxygen atoms;~~

~~R^9 is a member selected from the group consisting of H; (C_1-C_4) alkyl; (C_3-C_7) cycloalkyl; phenyl; benzyl; pyridyl; $C(=O)OR^{16}$; $C(=O)R^{16}$; OR^{16} ; (C_1-C_2) alkyl- OR^{16} ; and (C_1-C_2) alkyl- $C(=O)OR^{16}$; where R^{16} has the same meaning as defined above;~~

~~R^7_C is a member independently selected from the group consisting of the meanings of R^7_A and the meanings of R^7_B defined above;~~

~~—and further wherein—~~



(1.1.15)

~~comprises a saturated or unsaturated, 4 to 8 membered monocyclic, or 5 to 10 membered fused or open bicyclic, carbocyclic ring system containing a nitrogen heteroatom as shown in partial Formula (1.1.15); wherein optionally from 1 to 3 carbon atoms of said carbocyclic ring system may be individually replaced by a nitrogen heteroatom; or optionally 1 carbon atom thereof may be replaced by an oxygen heteroatom or by a sulfur heteroatom; or optionally 2 carbon atoms thereof may be individually replaced by a nitrogen heteroatom and an oxygen heteroatom, or by a nitrogen heteroatom and a sulfur heteroatom;~~

~~—where—~~

~~any moiety of partial Formula (1.1.15) recited above is optionally substituted with respect to (1) any one or more carbon atoms thereof, by a substituent R^{14} where R^{14} has the same meaning as defined above; (2) any one or more nitrogen atoms thereof by a substituent R^{15} where R^{15} has the same meaning as defined above, and all tautomer forms, and optionally N-oxide forms thereof; or (3) any sulfur atom thereof by 0, 1, or 2 oxygen atoms;~~

~~—and Z is further selected from—~~

~~(b) a moiety comprising a member selected from the group consisting of $-O-P(=O)(OH)_2$ (phosphoric); $-PH(=O)OH$ (phosphinic); $-P(=O)(OH)_2$ (phosphonic);~~

~~[P(=O)(OH)O(C₄-C₄)alkyl] (alkylphosphono); P(=O)(OH)O(C₄-C₄)alkyl (alkylphosphinyl); P(=O)(OH)NH₂ (phosphoramido); P(=O)(OH)NH(C₄-C₄)alkyl and P(=O)(OH)NHR²⁶ (substituted phosphoramido); O-S(=O)₂OH (sulfuric); S(=O)₂OH (sulfonic); S(=O)₂NHR²⁶ or NHS(=O)₂R²⁶ (sulfonamido) where R²⁶ is CH₃, CF₃, or o-tolyl; and acylsulfonamido selected from the group consisting of C(=O)NHS(=O)₂R²⁶; C(=O)NHS(=O)₂NH₂; C(=O)NHS(=O)₂(C₄-C₄)alkyl; C(=O)NHS(=O)₂NH(C₄-C₄)alkyl; C(=O)NHS(=O)₂N[(C₄-C₄)alkyl]₂; S(=O)₂NHC(=O)(C₄-C₄)alkyl; S(=O)₂NHC(=O)NH₂; S(=O)₂NHC(=O)NH(C₄-C₄)alkyl; S(=O)₂NHC(=O)N[(C₄-C₄)alkyl]₂; S(=O)₂NHC(=O)R²⁶; S(=O)₂NHCN; S(=O)₂NHC(=S)NH₂; S(=O)₂NHC(=S)NH(C₄-C₄)alkyl; S(=O)₂NHC(=S)N[(C₄-C₄)alkyl]₂; and S(=O)₂NHS(=O)₂R²⁶;~~

~~— where —~~

~~R²⁶ is H; (C₄-C₄)alkyl; phenyl; or OR¹⁸, where R¹⁸ has the same meaning as defined above;~~

~~provided that when Q⁴ is phenyl, R⁵ and R⁶ are taken together to form a moiety which is a member selected from the group consisting of partial Formulas (1.3.1), (1.3.2), (1.3.3) and~~



~~— or —~~

a pharmaceutically acceptable salt thereof.

2. - 5. (Canceled)

6. (Currently amended) A compound according to Claim 1 wherein Q¹ is phenyl or pyridyl; ~~◇◇ Q² is biphenyl, 3-phenyl-pyridine, cyclohexyl-benzene, [2,2']bipyridinyl, bicyclohexyl, naphthalene, or biphenylene; ◇◇ j is 1; ◇◇ m is 0 or 1; and ◇◇ n is 1; ◇◇ Z is a moiety selected from partial Formulas (1.1.1) through (1.1.3), (1.1.5), (1.1.6), and (1.1.10) through (1.1.14) where R⁷_A is (a) H, or CH₃ substituted by 0-3 R¹⁰ where R¹⁰ is F; or is CH₃ substituted by 0 or 1 R¹⁰ where R¹⁰ is CN, OR¹⁶ where R¹⁶ is CH₃ or CH₂CH₃, or NR¹⁶R¹⁷ or NR¹⁶C(=O)R¹⁷ where R¹⁶ and R¹⁷ are H or CH₃; (b) cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl; or (c) phenyl or benzyl substituted by 0-2 R¹⁰ where R¹⁰ is F, Cl, CF₃, CH₃, CH₂OH, SCH₃, CN, NO₂, OR¹⁶, or NR¹⁶R¹⁷ where R¹⁶ and R¹⁷ are H, CH₃, or CH₂CH₃; ◇◇ R⁹ is H or CH₃; ◇◇ W¹ is O; ◇◇ g is 1 and W² is O or CR²⁹R³⁰ where R²⁹ and R³⁰ are both H, or g is 0 and W² is thus absent; ◇◇ Y is C(R⁴_a); ◇◇ R¹_a is H, or F; ◇◇ R^A and R^B are independently H or CH₃; or R^A and R^B are taken together to form a (C₃-C₇)cycloalkyl-spiro-moiety; ◇◇ one of R^C and R^D is H and the other is H or CH₃; ◇◇ R⁴~~

and R² are H, F, or OCH₃; ~~and R³ is H or CH₃; and R⁴, R⁵ and R⁶ are H provided that R⁵ and R⁶ are not both H at the same time, F, Cl, OCH₃, CN, NO₂, or C(=O)R³ or C(=O)OR³ where R³ is CH₃; or R⁵ and R⁶ are taken together to form a moiety of partial Formula (1.3.1), (1.3.2), (1.3.3), (1.3.4), (1.3.11), (1.3.12), or (1.3.15) .~~

7. - 12. (Canceled)

13. (Currently amended) A compound according to Claim 1 wherein said compound is a member selected from the group consisting of the following:

~~4'-([2-(Benzo[2,1,3]thiadiazol-5-yloxy)-pyridine-3-carbonyl]-amino)-methyl)-biphenyl-4-yloxy]-acetic acid;~~

~~4'-([2-(Benzo[2,1,3]oxadiazol-5-yloxy)-pyridine-3-carbonyl]-amino)-methyl)-biphenyl-4-yloxy]-acetic acid;~~

~~4'-([2-(Benzo[1,3]dioxol-5-yloxy)-pyridine-3-carbonyl]-amino)-methyl)-biphenyl-4-yloxy]-acetic acid;~~

~~(±) 2-[4'-([2-(Benzo[1,3]dioxol-5-yloxy)-pyridine-3-carbonyl]-amino)-methyl)-2-fluoro-biphenyl-4-yloxy]-propionic acid;~~

~~(±) 2-(Benzo[1,3]dioxol-5-yloxy)-N-(2'-fluoro-4'-[1-(1H-tetrazol-5-yl)-ethoxy]-biphenyl-4-ylmethyl)-nicotinamide;~~

~~(±) 2-[4'-([2-(Benzo[1,3]dioxol-5-yloxy)-pyridine-3-carbonyl]-amino)-methyl)-3'-fluoro-biphenyl-2-yloxy]-propionic acid;~~

~~(±) 2-(Benzo[1,3]dioxol-5-yloxy)-N-(2'-fluoro-4'-[1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethoxy]-biphenyl-4-ylmethyl)-nicotinamide;~~

~~(±) N-[4'-(1-Carbamoyl-ethoxy)-2'-fluoro-biphenyl-4-ylmethyl]-2-(3-cyano-phenoxy)-nicotinamide;~~

~~(±) 2-[2,3'-Difluoro-4'-([2-(3-methoxy-phenoxy)-pyridine-3-carbonyl]-amino)-methyl)-biphenyl-4-yloxy]-propionic acid;~~

~~2-(Benzo[1,3]dioxol-5-yloxy)-N-(4'-carbamoylmethyl-3-fluoro-biphenyl-4-ylmethyl)-nicotinamide;~~

~~2-(Benzo[1,3]dioxol-5-yloxy)-N-(4'-[2-cyano-benzoylamino)-methyl]-2'-fluoro-biphenyl-4-ylmethyl)-5-fluoro-nicotinamide;~~

~~Pyridine-2-carboxylic acid-(3'-fluoro-4'-[2-(4-fluoro-phenoxy)-nicotinamide]-methyl)-biphenyl-4-ylmethyl)-amide;~~

~~2-(Benzo[1,3]dioxol-5-yloxy)-N-(2'-fluoro-4'-[1-methyl-1-(1H-tetrazol-5-yl)-ethyl]-biphenyl-4-ylmethyl)-nicotinamide;~~

~~5-Fluoro-N-(3-fluoro-4'-[5-methyl-4H-[1,2,4]triazole-3-carbonyl]-amino)-methyl)-biphenyl-4-ylmethyl)-2-(3-methoxy-phenoxy)-nicotinamide;~~

~~2-(Benzo[1,3]dioxol-5-yloxy)-N-(2'-fluoro-4'-((2-methoxy-benzoylamino)-methyl)-biphenyl-4-ylmethyl)-nicotinamide;~~

~~N-[4'-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2'-fluoro-biphenyl-4-ylmethyl]-2-(4-fluoro-phenoxy)-nicotinamide;~~

~~N-(2'-Fluoro-4'-(((3H-imidazole-4-carbonyl)-amino)-methyl)-biphenyl-4-ylmethyl)-2-(3-nitro-phenoxy)-nicotinamide;~~

~~(±)-3-[4'-(((2-(3-Chloro-4-fluoro-phenoxy)-pyridine-3-carbonyl)-amino)-methyl)-2-fluoro-biphenyl-4-yloxy]-butyric acid;~~

~~2-[4'-(((2-Benzo[2,1,3]thiadiazol-5-yloxy)-pyridine-3-carbonyl)-amino)-methyl]-2-fluoro-biphenyl-4-yl]-2-methyl-propionic acid;~~

~~(±)-2-[4'-(((2-(Benzo[2,1,3]oxadiazol-5-yloxy)-pyridine-3-carbonyl)-amino)-methyl)-2-fluoro-biphenyl-4-yloxy]-propionic acid; and~~

~~(±)-2-[3'-Fluoro-4'-((2-(2-methyl-2H-benzotriazol-5-yloxy)-pyridine-3-carbonyl)-amino)-methyl]-biphenyl-4-yloxy]-propionic acid;~~

~~2-(3-Cyano-phenoxy)-N-(2'-fluoro-4'-((pyridin-2-ylmethyl)-carbameoyl)-biphenyl-4-ylmethyl)-nicotinamide;~~

~~2-(Benzo[1,3]dioxol-5-yloxy)-N-(2'-fluoro-4'-((quinolin-2-ylmethyl)-carbameoyl)-biphenyl-4-ylmethyl)-nicotinamide;~~

~~5-Fluoro-2-(4-fluoro-phenoxy)-N-[3-fluoro-3'-(1H-tetrazol-5-yl)-biphenyl-4-ylmethyl]-nicotinamide;~~

~~N-[3-Fluoro-4'-((1-hydroxy-pyridin-2-ylmethyl)-carbameoyl)-biphenyl-4-ylmethyl]-2-(3-methoxy-phenoxy)-nicotinamide;~~

~~(±)-N-[3-Fluoro-4'-(2-hydroxy-1,2-dimethyl-propoxy)-biphenyl-4-ylmethyl]-2-(4-fluoro-phenoxy)-nicotinamide;~~

~~N-[2'-Fluoro-4'-(1-hydroxy-1-methyl-ethyl)-biphenyl-4-ylmethyl]-2-(4-fluoro-phenoxy)-nicotinamide; and~~

~~2-(3-Chloro-4-fluoro-phenoxy)-N-[4'-(pyridin-2-ylmethoxy)-biphenyl-4-ylmethyl]-nicotinamide.~~

14. - 18. (Canceled)

19. (Withdrawn) A method of treating a disease, disorder or condition mediated by the PDE4 isozyme in a mammal, said method comprising administering to said mammal in need of such mediation, a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt thereof.

20. (Withdrawn) A method of claim 19 wherein said PDE4 isozyme is the PDE4-D subtype isozyme.

21. (Withdrawn) A method of claim 19 wherein said disease, disorder or condition is atopic asthma; non-atopic asthma; allergic asthma; bronchial asthma; essential asthma; true asthma; intrinsic asthma caused by pathophysiologic disturbances; extrinsic asthma caused by environmental factors; essential asthma of unknown or inapparent cause; bronchitic asthma; emphysematous asthma; exercise-induced asthma; occupational asthma; infective asthma caused by bacterial, fungal, protozoal or viral infection; non-allergic asthma; incipient asthma; or wheezy infant syndrome.

22. (Withdrawn) A method of claim 19 wherein said disease, disorder or condition is chronic or acute bronchoconstriction; chronic bronchitis; small airways obstruction; emphysema; pneumoconiosis; chronic eosinophilic pneumonia; chronic obstructive pulmonary disease; adult respiratory distress syndrome; or exacerbation of airways hyper-reactivity consequent to other drug therapy.

23. (Withdrawn) A method of claim 22 wherein said chronic obstructive pulmonary disease is characterized by irreversible, progressive airways obstruction.

24. (Withdrawn) A method of claim 22 wherein said pneumoconiosis is aluminosis; bauxite workers' disease; anthracosis; miners' disease; asbestosis; steam-fitters' asthma; chalicosis; flint disease; ptilosis caused by inhaling the dust from ostrich feathers; siderosis caused by the inhalation of iron particles; silicosis; grinders' disease; byssinosis; cotton-dust asthma; or talc pneumoconiosis.

25. (Withdrawn) A method of claim 19 wherein said disease, disorder or condition is bronchitis; acute bronchitis; chronic bronchitis; acute laryngotracheal bronchitis; arachidic bronchitis; catarrhal bronchitis; croupus bronchitis; dry bronchitis; infectious asthmatic bronchitis; productive bronchitis; staphylococcus bronchitis; streptococcal bronchitis; or vesicular bronchitis.

26. (Withdrawn) A method of claim 19 wherein said disease, disorder or condition is bronchiectasis; cylindric bronchiectasis; sacculated bronchiectasis; fusiform bronchiectasis; capillary bronchiectasis; cystic bronchiectasis; dry bronchiectasis or follicular bronchiectasis.

27. (Withdrawn) A method of claim 19 wherein said disease, disorder or condition is seasonal allergic rhinitis; perennial allergic rhinitis; sinusitis; purulent sinusitis; nonpurulent sinusitis; acute sinusitis; chronic sinusitis; ethmoid sinusitis; frontal sinusitis; or sphenoid sinusitis.